

REMARKS

Claims 2-6, 8-14, 16, 20, 22, 26-28, 31, 33-36, and 40-70 were previously pending in this Application. Claims 3, 6, 8-11, 13, 20, 22, 34-36, 40-44, 59-63, and 66-70 were previously withdrawn from consideration by the Examiner. Claims 1, 7, 15, 17-19, 21, 23-25, 29, 30, 32, and 37-39 were previously canceled. By this Amendment, claims 2, 4, and 5 have been amended, and claims 3, 6, 8-11, 13, 20, 22, 40-44, 59-63, 66, 67, and 70 have been canceled. As a result, claims 2, 4, 5, 12, 14, 16, 26-28, 31, 33-36, 45-58, 64, 65, 68, and 69 are pending for examination. No new matter has been added to the present Application by this Amendment.

Each of the rejections levied in the outstanding Office Action is addressed individually below.

Claim objections

Claims 14-25 were objected to under 37 CFR § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from a multiple dependent claim. Applicant notes that this issue was resolved in the Preliminary Amendment of September 21, 2006. Currently, claims 14 and 16 only depend from one claim. Applicant therefore respectfully requests the removal of this objection.

Rejection of Claims under 35 U.S.C. § 112, first paragraph

Claims 2-5, 8, 12-14, 16, 26, 28, 33, 37, 40-58, 64, and 65 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification, while being enabling for some of the claimed compounds, does not reasonably provide enablement for the full scope of the claims. The Examiner alleges that “[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.” Applicant respectfully disagrees.

The specification enables one of ordinary skill in the art to make the claimed invention.

Applicant believes the amended claims are enabled. Upon review of Reaction Schemes I-IX (on pages 60-72), the 68 representative synthetic examples (on pages 77-180), and the exemplary

compounds (on pages 180-191) of the specification, one of ordinary skill in the art could make the claimed compounds without undue experimentation.

The specification enables one of ordinary art to use the claimed compounds.

Section 2164.01(c) of the MPEP entitled “*How to Use the Claimed Invention*” sets forth the requirement for enabling the use of the claimed invention:

“If a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. § 112 is satisfied. *In re Johnson*, 282 F.2d 370, 373, 127 USPQ 216, 219 (CCPA 1960); *In re Hitchings*, 342 F.2d 80, 87, 144 USPQ 637, 643 (CCPA 1965). See also *In re Brana*, 51 F.2d 1560, 1566, 34 USPQ2d 1437, 1441 (Fed. Cir. 1993).

“[W]hen a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for non-enablement based on how to use.”

The Application, as filed, teaches one of ordinary skill in the art how to use the claimed compounds. The specification teaches that the compounds of the invention “are useful, for example, as immune response modifiers (IRMs) due to their ability to modulate cytokine biosynthesis ... and otherwise modulate the immune system when administered to animals” (page 3, lines 3-6, of the published international PCT application no. WO 2005/094531). The Application also teaches (on pages 191-193) experimental procedures to assess the induction of cytokine biosynthesis in human cells by the claimed compounds. Therefore, the requirement for enabling the use of the claimed compounds under § 112 is satisfied. The Examiner has not provided any evidence that the claimed compounds could not be used for the stated purpose. Applicant therefore respectfully requests the removal of this rejection.

Rejection of Claims 1-5, 7, 8, 12, 13-33, and 37 under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-5, 7, 8, 12, 13-33, and 37 as being unpatentable over Japanese patent publication no. JP 11[1999]-222432 to Iizuka *et al.* ("Iizuka"), in view of Wermuth *et al.* "Molecular variations based on isosteric replacements." *The Practice of Medicinal Chemistry*, pp. 203-237, 1996 ("Wermuth"). Applicant respectfully disagrees.

Applicant asserts that the claimed invention is not obvious in view of the cited art because the above-mentioned combination of references does not support a *prima facie* case of obviousness. Applicant does not agree with the Examiner's rejection because (1) the structural differences between the claimed compounds and those of Iizuka is significant and not obvious; and (2) the cited references do not teach or suggest modification of Iizuka's compounds to those claimed in the present Application.

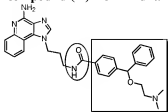
The Federal Circuit recently ruled that a structural similarity *and* some motivation in the prior art are both required to establish a *prima facie* case of obviousness in the chemical arts. *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007). Applicant respectfully contends that the Examiner's rejection does not satisfy these two requirements.

We have held that "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness." *Dillon*, 919 F.2d at 692. In addition to structural similarity between the compounds, a *prima facie* case of obviousness also requires a showing of "adequate support in the prior art" for the change in structure. *In re Grabiak*, 769 F.2d 729, 731-32 (Fed. Cir. 1985).

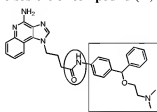
The claimed compounds and those of Iizuka are structurally dissimilar, as shown below. Iizuka uses an amide linkage with the orientation -NH-CO- to join an imidazoquinoline moiety and a benzhydryl moiety. The claimed imidazoquinoline compounds differ from the imidazoquinoline-benzhydryl compounds of Iizuka in two significant ways. First, the claimed imidazoquinoline compounds do not include a benzhydryl moiety. Second, the amide linkage of the claimed imidazoquinoline compounds has the opposite orientation, -CO-NH-, relative to the amide linkage

of Iizuka's compounds. Neither Iizuka nor Wermuth teaches or suggests the two changes necessary to modify Iizuka's compounds to the claimed compounds of the present Application.

compound (II) from Iizuka



bioisostere of compound (II) from Iizuka

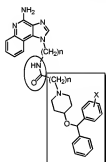


The Examiner alleges that Wermuth provides the motivation necessary to convert Iizuka's compounds to the claimed compounds of the present Application. Applicant disagrees. Wermuth teaches that the inversion of amide groups within several classes of bioactive compounds might yield bioisosteric analogs which maintain biological activity and reduce unwanted side effects. The compounds of Wermuth do not resemble the imidazoquinoline compounds of Iizuka or the present invention. Accordingly, one of ordinary skill in the art can not apply the teachings of Wermuth to the imidazoquinoline compounds of Iizuka with a reasonable expectation of success. Yet, even if one does apply the teachings of Wermuth to the imidazoquinoline compounds of Iizuka, the compounds that result remain structurally dissimilar from those which are claimed. This is so because Wermuth does not teach both changes which are necessary to convert Iizuka's imidazoquinoline compounds to the claimed compounds. Regardless of the orientation of the amide linkage, the imidazoquinoline compounds of Iizuka retain the benzhydryl moiety. Iizuka's imidazoquinoline compounds are structurally dissimilar from the claimed imidazoquinolines.

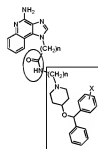
As mentioned, structural similarity *and* some motivation in the prior art are both required to establish a *prima facie* case of obviousness in the chemical arts. After applying the teachings of Wermuth to the imidazoquinoline compounds of Iizuka one does not arrive at the claimed compounds of the present Application because Wermuth does not teach or suggest changing the benzhydryl moiety of Iizuka's compounds. The Examiner's rejection under § 103 is untenable because the cited art fails to teach or suggest how one of ordinary skill could arrive at the claimed compounds of the present Application from those of Iizuka. Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness based upon the combined teachings of Iizuka and Wermuth. Accordingly, Applicant requests that the rejection under § 103 be removed.

The Examiner has also rejected claims 1-5, 7, 8, 12, 13-33, and 37 as being unpatentable over Japanese patent application no. JP 09208584 to Namba *et al.* ("Namba"), in view of Wermuth. Applicant respectfully disagrees for the same reasons that were applied to Iizuka, in view of Wermuth. As reasoned above, Applicant submits that the Examiner has not established a *prima facie* case of obviousness based upon the combined teachings of Namba and Wermuth. The claimed imidazoquinoline compounds differ from the imidazoquinoline compounds of Namba in two significant ways. First, the claimed imidazoquinoline compounds are not linked to benzhydryl moieties. Second, the R₁ amide linkages of the claimed imidazoquinoline compounds has the opposite orientation, -CO-NH-, relative to the amide linkages of Namba.

compound (I) from Namba



bioisostere of compound (I) from Namba



Namba does not teach or suggest the two changes necessary to modify Namba's imidazoquinoline compounds to the claimed compounds of the present Application. Wermuth does not cure the deficiencies of Namba because Wermuth also fails to teach or suggest the two modifications necessary to convert Namba's imidazoquinoline-benzhydryl compounds to the claimed compounds. Specifically, Wermuth does not teach or suggest the change of the benzhydryl moiety of Namba's compounds to the substituents claimed in the present Application. The Examiner's rejection under § 103 is untenable because the cited art fails to teach or suggest how one of ordinary skill could arrive at the instant compounds from the imidazoquinoline compounds of Namba. Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness based upon the combined teachings of Namba and Wermuth. Accordingly, Applicant requests that the rejection under § 103 be removed.

Provisional Double Patenting Rejection of Claims 2 and 33

The Examiner made the provisional rejection of claim 2 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending U.S. patent application, U.S.S.N. 11/595,895. As this is a provisional rejection, Applicant wishes to refrain from addressing this rejection until it matures into an actual rejection.

The Examiner made the provisional rejection of claim 33 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending U.S. patent application, U.S.S.N. 11/883,665. As this is a provisional rejection, Applicant wishes to refrain from addressing this rejection until it matures into an actual rejection.

The Examiner made the provisional rejection of claim 33 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending U.S. patent application, U.S.S.N. 11/595,049. As this is a provisional rejection, Applicant wishes to refrain from addressing this rejection until it matures into an actual rejection.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 23/2825, under Docket No. C1271.70044US02, from which the undersigned is authorized to draw.

Dated: February 8, 2010

Respectfully submitted,

By /C. Hunter Baker/
C. Hunter Baker, M.D., Ph.D.
Registration Number: 46,533
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000